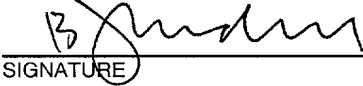


FORM PTO-1390 (REV 11-98)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER 1579-527
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5) 09/762097 Unknown
INTERNATIONAL APPLICATION NO. PCT/US99/17678	INTERNATIONAL FILING DATE 5 August 1999	PRIORITY DATE CLAIMED 6 August 1998
TITLE OF INVENTION URATE OXIDASE		
APPLICANT(S) FOR DO/EO/US Michael HERSHFIELD and Susan J. KELLY		
<p>Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:</p> <p>1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).</p> <p>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.</p> <p>5. A copy of the International Application as filed (35 U.S.C. 371(c)(2)).</p> <p>a. <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau).</p> <p>b. <input checked="" type="checkbox"/> has been transmitted by the International Bureau.</p> <p>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</p> <p>6. <input type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)).</p> <p><input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau).</p> <p>b. <input type="checkbox"/> have been transmitted by the International Bureau.</p> <p>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</p> <p>d. <input type="checkbox"/> have not been made and will not be made.</p> <p>8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (U.S.C. 371(c)(3)).</p> <p>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p> <p>Items 11. To 16. Below concern document(s) or information included:</p> <p>11. <input type="checkbox"/> An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98.</p> <p>12. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. 3.28 and 3.31 is included.</p> <p>13. <input type="checkbox"/> A FIRST preliminary amendment. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment.</p> <p>14. <input type="checkbox"/> A substitute specification.</p> <p>15. <input type="checkbox"/> A change of power of attorney and/or address letter.</p> <p>16. <input checked="" type="checkbox"/> Other items or information. PTO-1449 and copy of International Search Report <input checked="" type="checkbox"/> This application is entitled to "Small entity" status. <input checked="" type="checkbox"/> Two "Small entity" statements attached.</p>		



U.S. APPLICATION NO. (if known, see 37 C.F.R. 1.5) 084762097		INTERNATIONAL APPLICATION NO PCT/US99/17678		ATTORNEY'S DOCKET NUMBER 1579-527				
17. <input checked="" type="checkbox"/> The following fees are submitted:				CALCULATIONS PTO USE ONLY				
BASIC NATIONAL FEE (37 C.F.R. 1.492(a)(1)-(5)): -- Neither international preliminary examination fee (37 C.F.R. 1.482) nor international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO\$1000.00 -- International preliminary examination fee (37 C.F.R. 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO\$860.00 -- International preliminary examination fee (37 C.F.R. 1.482) not paid to USPTO but international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO\$710.00 -- International preliminary examination fee paid to USPTO (37 C.F.R. 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)\$690.00 -- International preliminary examination fee paid to USPTO (37 C.F.R. 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)\$100.00 <div style="text-align: right;">ENTER APPROPRIATE BASIC FEE AMOUNT =</div> Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 C.F.R. 1.492(e)).								
						\$	690.00	
						\$	0.00	
CLAIMS		NUMBER FILED	NUMBER EXTRA	RATE				
Total Claims		17	-20 = 0	X	\$18.00	\$ 0.00		
Independent Claims		4	-3 = 1	X	\$80.00	80.00		
<input checked="" type="checkbox"/> MULTIPLE DEPENDENT CLAIMS(S) (if applicable)				\$270.00	\$ 0.00			
TOTAL OF ABOVE CALCULATIONS =				\$	770.00			
Reduction by 1/2 for filing by small entity, if applicable. Small entity status must also be asserted. (Note 37 C.F.R. 1.9, 1.27, 1.28).					385.00			
SUBTOTAL =				\$	385.00			
Processing fee of \$130.00, for furnishing the English Translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 C.F.R. 1.492(f)).				+	0.00			
TOTAL NATIONAL FEE =				\$	385.00			
Fee for recording the enclosed assignment (37 C.F.R. 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. 3.28, 3.31). \$40.00 per property				+	\$ 40.00			
Fee for Petition to Revive Unintentionally Abandoned Application (\$1240.00 - Small Entity = \$620.00)				\$	0.00			
TOTAL FEES ENCLOSED =				\$	425.00			
				Amount to be:				
				refunded	\$			
				Charged	\$			
a. <input checked="" type="checkbox"/> A check in the amount of \$425.00 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. 14-1140 in the amount of \$_____ to cover the above fees. A duplicate copy of this form is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-1140. A duplicate copy of this form is enclosed. d. <input type="checkbox"/> The entire content of the foreign application(s), referred to in this application is/are hereby incorporated by reference in this application. NOTE: Where an appropriate time limit under 37 C.F.R. 1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. 1.137(a) or (b)) must be filed and granted to restore the application to pending status.								
SEND ALL CORRESPONDENCE TO: NIXON & VANDERHYE P.C. 1100 North Glebe Road, 8 th Floor Arlington, Virginia 22201 Telephone: (703) 816-4000								
				 SIGNATURE				
				B. J. Sadoff NAME				
				36,663 REGISTRATION NUMBER				
				February 2, 2001 Date				

URATE OXIDASE

The present application claims benefit of U.S. Provisional Application No. 60/095,489, filed August 6, 1998, the entire contents of which is incorporated herein by reference.

5 The invention disclosed herein was made with U.S. Government support under Grant No. DK48529, awarded by the National Institutes of Health. The Government has certain rights in the invention.

The present invention relates, in general, to urate oxidase (uricase) proteins and nucleic acid molecules encoding same. In particular, the invention relates to uricase
10 proteins which are particularly useful as, for example, intermediates for making improved modified uricase proteins with reduced immunogenicity and increased bioavailability. The preferred modified uricase proteins of the present invention include the uricase proteins covalently bound to poly(ethylene glycols) or poly(ethylene
15 oxides). The present invention provides, therefore, uricase proteins, antibodies which specifically bind with the proteins, nucleic acid molecules encoding the uricase proteins and useful fragments thereof, vectors containing the nucleic acid molecules, host cells containing the vectors and methods of using and making the uricase proteins and nucleic acid molecules.

Background

20 Gout is the most common inflammatory joint disease in men over age 40 (Roubenoff 1990). Painful gouty arthritis occurs when an elevated blood level of uric acid (*hyperuricemia*) leads to the episodic formation of microscopic crystals of monosodium urate monohydrate in joints. Over time, chronic hyperuricemia can also result in destructive crystalline urate deposits (*tophi*) around joints, in soft tissues, and
25 in some organs (Hershfield 1996). Uric acid has limited solubility in urine and when overexcreted (*hyperuricosuria*) can cause kidney stones (*uricolithiasis*). In patients with certain malignancies, particularly leukemia and lymphoma, marked hyperuricemia and hyperuricosuria (due to enhanced tumor cell turnover and lysis during chemotherapy) pose a serious risk of acute, obstructive renal failure (Sandberg et al. 1956; Gold and
30 Fritz 1957; Cohen et al. 1980; Jones et al. 1990). Severe hyperuricemia and gout are associated with renal dysfunction from various causes, including cyclosporine therapy to